

Stewart (D. D.)

HYDRO-NAPHTHOL IN THE PROPHYLAXIS AND
TREATMENT OF CHOLERA: REPORT OF
LABORATORY EXPERIMENTS.

BY

D. D. STEWART, M.D.,

CLINICAL LECTURER ON MEDICINE IN THE JEFFERSON MEDICAL COLLEGE.



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IN a preliminary note as to the prophylaxis and treatment of cholera, published in THE MEDICAL NEWS of September 17th, I suggested the use of hydro-naphthol both as a preventive and as a remedy for the developed disease, it having occurred to me, from several years' experience with this drug in intestinal affections of bacterial origin, that it would probably fulfil the indications of antiseptic and germicide far better than salol. It will be remembered that salol has lately been rendered somewhat popular as a cholera remedy through the writings of Löwenthal, who discovered that it possessed toxic power over comma-spirilla, under the influence of pancreatic juice, which dissociated it into its components, salicylic acid and phenol. It occurred to me that the latter, which exists in salol in the proportion of 36 per cent., was in all probability the active agent, as it is, of course, a far more efficient germicide than the former, and on comma-spirilla has an especially lethal effect, as these perish in a one-half per cent. solution, as was shown by Koch.

As I pointed out, the experiments of Löwenthal,



though interesting and demonstrating the effect of nascent phenol on comma-spirilla in the test-tube, are unfortunately, of little practical utility, for the reason that it is not in the duodenum but in the lower part of the ileum that the contagium finds lodgment and exerts its specific effect. Salol undergoes decomposition in the upper part of the jejunum, and is there promptly converted into soluble, *absorbable*, and very questionable antiseptic salts, sodium salicylate and carbolate, little undecomposed salol reaching the lower segment of the bowel, unless the intestinal contents are abnormally acid or the drug is ingested in doses the effect of which would be very injurious.

A remedy to be directed with effect against the contagium of cholera should be a more or less ideal intestinal antiseptic; it should be but slightly soluble and decomposable, yet a germicide in aqueous solution, and both non-toxic and non-irritant in doses sufficient to produce a germicidal action. Experiments with naphthalin as an intestinal antiseptic, clinical and laboratory, have been disappointing. In recent years it has almost ceased to be used, hydro-naphthol or beta-naphthol¹ taking its place.

¹ Beta-naphthol and hydro-naphthol, which in their powdered condition are very similar in physical appearance, are regarded by some chemists as identical bodies. This, however, would appear not to be the case, there being a number of points of distinction between them. Hydro-naphthol is said to possess a different molecular arrangement from beta-naphthol, from which it is derived by the substitution of a molecule of hydroxyl (OH) for an atom of H. While naphthalin ($C_{10}H_8$) is formed by the union of two benzol groups saturated with hydrogen, beta-naphthol ($C_{10}H_7(OH)$) may be stated to equal naphthalin in which a

It occurred to me that hydro-naphthol would perhaps fulfil the desired indications. It had been found of signal service in intestinal affections, especially in those of bacterial origin. It is related to phenol, being, like it, a benzol derivative; hence, presumably, cholera-spirilla might also be vulnerable to it. It is but slightly soluble in aqueous solutions, is non-irritant and non-poisonous, and does not readily undergo decomposition; it would, therefore, be carried unchanged to the affected part of the bowel, even in moderate doses, without absorption occurring. To determine its actual value as an antiseptic and germicide in cholera, I asked Dr. Ghriskey, of the Laboratory of Hygiene, University of Pennsylvania, to undertake some experiments as to its influence on pure cultures of comma-spirilla. The following is a brief account of the result; the details of the experiments are to be subsequently published, embodied in the annual report of the Hygienic Laboratory work:

molecule of hydroxyl has been substituted for an atom of H. Hydro-naphthol would represent naphthalin in which two molecules of hydroxyl are substituted for two atoms of H. Beta-naphthol, which is probably by no means as toxic and unsafe for internal administration as Seabury and Johnson assert, will perhaps also be found of value in cholera. Dr. Ghriskey is now investigating its action on comma-spirilla for me. It is, like hydro-naphthol, unquestionably a valuable intestinal antiseptic. M. Bouchard's experiments with it (see *N. Y. Medical Record*, Dec. 12, 1887, p. 797) indicate that it is only toxic in enormous doses, being less so than naphthalin, the much weaker antiseptic. Bouchard found that a lethal dose for a man of 130 pounds avoird., was about 250 grams (equivalent to a half-pound). Toxic effects (albuminuria, spasmodic muscular contractions, salivation, and coma) were produced only when naphthol was ingested in doses of about 26 grams.

THE LABORATORY OF HYGIENE,
UNIVERSITY OF PENNSYLVANIA.
September 23, 1892.

DR. DAVID D. STEWART,

DEAR DOCTOR: The laboratory experiments to determine whether hydro-naphthol possesses any antiseptic or germicidal action against the Asiatic cholera-spirillum of Koch, which were undertaken at your request, have been completed, and we herewith send you a report of the results obtained. The pure cultures of the organism used in our experiments were derived from one originally secured from the Bureau of Animal Industry, Washington, D. C. In its morphology and behavior in nutritive culture-media it was shown to be identical with the comma-spirillum of Koch, though we cannot vouch for its virulence.

We found in a series of experiments, repeated with constant results, that in solutions of a strength of 1 part hydro-naphthol and 7000 parts nutritive culture-medium, the drug proved to be distinctly antiseptic. It was also demonstrated that with a mixture of equal parts of a saturated aqueous solution of hydro-naphthol and a bouillon-culture of this organism, the drug was germicidal within five minutes. In this series the results were invariably the same.

Two samples of hydro-naphthol were employed by us: the one which you sent us, another sold by Seabury & Johnson, N. Y. The solubility, determined by the usual method, showed some variance in the two preparations; in general, we found the solubility to be in the proportion of from 1 part in 1000 to 1 part in 900 of cold distilled water.

In so far as the experiments of the *antiseptic* value of hydro-naphthol are concerned, they are corroborative of results obtained by Abbott and published by Fowler, of Brooklyn, N. Y., in 1885. These experiments were made with the bacillus anthracis and the bacillus subtilis. Both are known to be far more resistant to antiseptic and germicidal agents than the comma-spirillum, which

is an organism classed among those least resistant. The results of the *disinfective* action of hydro-naphthol do not coincide with the results obtained by Abbott. This may in part be explained by the nature of the organisms with which the work was done, but more probably was due to the improvements in the technique of the experiments as practised to-day over the methods used at the date of Abbott's experiments.

Very truly yours,

ALBERT A. GHRISKEY, M.D.,

Assistant in Bacteriology.

The foregoing report indicates that I was correct in my surmises regarding the probable value of hydro-naphthol, both as a prophylactic agent and as a remedy for developed cholera. It would appear, indeed, that we very likely have in it a medicament of extraordinary value, for it has thus been actually demonstrated beyond question that a proportion as high as one to seven thousand has an undoubted inhibiting effect on the development of the comma-spirillum, and that a proportion of about one to two thousand (equal parts aqueous solution and culture medium) exerted a prompt germicidal action.¹ As one part to seven thousand equals about a grain to the pint, or to the avoirdupois pound, and as the contents of the small intestine, when the latter in its entire length is thoroughly distended, cannot amount to more than nine or ten pints, it would follow that, under any condition, but ten grains of hydro-naphthol, if in solution, would be required to

¹ Time did not permit carrying the experiments farther, to ascertain if a less percentage of hydro-naphthol is germicidal. This is now being done. The result will be published subsequently with the results of a study of beta-naphthol.

render the entire small intestine antiseptic against the comma-spirillum, preventing its development, while about forty grains, under similar conditions, would disinfect the intestine, promptly killing any spirilla present. Despite these calculations, it is, of course, somewhat difficult to accurately formulate the exact dose necessary to create immunity against cholera, or that sufficient to exert a bactericidal effect in cases of the developed disease. Fortunately we have in hydro-naphthol one that is non-toxic in doses probably much larger than would be sufficient for the latter effect. In cases of simple diarrhea, in dysentery, and in enteric fever, I have frequently administered a half-dram in the twenty-four hours, continuing this often for weeks, totally without effect other than beneficial, and it is quite certain that doses much larger than these may be similarly used. The slight inhibition of gastric digestion that hydro-naphthol produces is readily obviated by the administration of the latter in keratin-coated pills, which are soluble in the duodenum, or if the drug is ingested in powder, capsule, wafer, or emulsion, by taking it between meals. It is without effect on duodenal digestion.

As a prophylactic against cholera when, from exposure, the disease seems imminent, hydro-naphthol should be taken in doses of from eight to ten grains four times daily for three or four days, and, subsequently, in from five- to eight-grain doses with the same frequency. This amount will probably at once exert an antiseptic effect, and at the expiration of twenty-four hours be germicidal. In early choleraic diarrhea it should be used in quantities of ten

grains hourly, or even half-hourly, until from one to two drams have been taken. Here it may be, and, deed, by choice, should be, combined with an opiate. An overwhelming testimony exists as to the extraordinary benefit likely to accrue from a prompt resort to opium in the stage of preliminary diarrhea, Sir George Johnson's most dangerous theoretic views to the contrary notwithstanding. The extended experience of Sir Thomas Watson, Fergus, of Glasgow; Aitkin, Macpherson, Twining, Parkes, our own Flint, Sr., and many others who have passed through several epidemics, leaves no doubt as to the great utility of opium. Nevertheless, as pointed out in my former paper, treatment by opium is only symptomatic, for this drug can neither destroy the comma-bacillus nor retard its development. Opium apparently acts in early choleraic diarrhea by checking the bowel-irritation caused by the spirillum or its leukomaïne. If, conjointly, a second remedy can be administered that will have a lethal effect on the spirillum the ideal treatment of cholera, at least in its early stage, has been found.

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